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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/367,794	01/06/2000	DAVID S. DIME	018148-00013	4773

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/367,794	Applicant(s) DIME ET AL.	
	Examiner Chih-Min Kam	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *1-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4)☒ Interview Summary (PTO-413) Paper No(s). *13* .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, claims 44-66, and a drug of a local anesthetic, a protein of sodium channel, and an anchoring group of a sulfhydryl-reactive group in Paper No. 12 is acknowledged. Claims 46, 53 and 62 have been amended. The traversal is on the ground(s) that there is a technical relationship among the claimed inventions involving one or more special technical features, thus unity of invention exists. This is not found persuasive because Group I and Group II have different method steps and different outcomes, thus they do not have the same technical features. Accordingly, the claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single inventive concept and lack of unity is deemed proper.

Informalities

The disclosure is objected to because of the following informalities:

2. The brief description of Fig. 5 (page 4, lines 9-26) does not match with the drawings. For example, there are Fig. 5A-Fig. 5H in the drawings, however, only Fig. 5A-Fig. 5D are described. Appropriate correction is required.

3. The brief description of Fig. 8 (page 5, lines 14-22) does not match with the drawings. For example, there is a drawing for $C_{13}°$, but the description indicates it is $C_{14}°$. Appropriate correction is required.

4. At page 16, line 20, the text indicates Figure 1D, however, there is no Figure 1D in the drawing. Appropriate correction is required.

5. At page 17, line 25, the text indicates Figure 1E, however, there is no Figure 1E in the drawing. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 44-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-66 are indefinite because of the use of the term "a chemically reactive group". The term "a chemically reactive group" renders the claim indefinite, it is unclear what group is as to a chemically reactive group. Claims 45-51, 53-58 and 60-66 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

7. Claims 46, 49, 50, 53, 56, 57, 62, 65 and 66 are indefinite because the claim contains non-elected inventions.

8. Claim 46 is indefinite because the drug in the claim is cited as a local anesthetic, which does not contain anchoring moiety, however, the independent claim 44 cites the drug having anchoring moiety.

9. Claims 47, 54 and 63 are indefinite because of the use of the term "said biological target molecule is on a protein". The term "said biological target molecule is on a protein" renders the claim indefinite, it is unclear what molecule is as to the biological target molecule on a protein, and how the biological target molecule is related to the protein.

10. Claims 50, 57 and 66 are indefinite because of the use of the term "a dithiopyridyl group, a reactive disulfide". The term "a dithiopyridyl group, a reactive disulfide" renders the claim indefinite, it is not clear dithiopyridyl group and the reactive disulfide are mutually exclusive since dithiopyridyl group is a reactive disulfide.

11. Claim 51 recites the limitation "said compound" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 51 is also indefinite because of the use of the terms "A is a drug" and "D is a drug", it is not clear which component in the formula is a drug.

12. Claim 52 recites the limitation "with a compound" in line 5. There is insufficient antecedent basis for this limitation in the claim. Claim 52 is indefinite because the claim recites "said anchoring moiety reacts with the chemically reactive group of the target molecule to form a covalent bond" in step (b), and "the drug, D, that forms a covalent bond with the chemically reactive group" in step (d), it is not clear which component, A or D, forms covalent bond with the chemically reactive group. It is also unclear which compound, the whole molecule (A-L-D) or D is identified as a drug.

13. Claim 58 is indefinite because of the use of the term "said biological target molecule comprises a protein target and a bifunctionally chemically reactive group". The term "said biological target molecule comprises a protein target and a bifunctionally chemically reactive group" renders the claim indefinite, it is unclear where the bifunctionally chemically reactive group is located in the biological target molecule, and whether the bifunctionally chemically reactive group is different from the chemically reactive group of claim 52.

14. Claim 59 recites the limitations "on a protein" in lines 3 and 7, and "on said protein" in lines 4 and 9. There is insufficient antecedent basis for this limitation. It is also unclear which compound, the whole molecule (A-L-D), A (the first drug) or D (the second drug) is identified as a drug.

15. Claim 65 recites the limitations "said anchoring moiety" in line 1. There is insufficient antecedent basis for this limitation.

Claim Rejections - 35 USC § 102/103(a)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 44, 47 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Greenfield *et al.* (EP 0398305).

Greenfield *et al.* teach a conjugate of anthracycline with a cell reactive molecule such as antibody or a ligand of EGF or bombesin (an anchoring group) via a linker and a method for delivering the cytotoxic anthracyclines to eliminate a selected population of cells (abstract; page 4, lines 49-51; page 7, lines 41-44; claims 44, 47 and 51). The antigen and EGF receptors are

proteins where the side chains of amino acid residues such as amino, carboxyl and thiol groups are chemically reactive groups. The antibodies of the conjugate bind tumor-associated antigen (page 8, lines 19-23) and the ligand EGF of the conjugate bind the EGF receptors of the tumor cell (page 8, lines 43-50). Thus, the reference makes obvious if not anticipated to the claimed method for identifying a drug containing an anchoring moiety, which binds a target site of a biological molecule.

18. Claims 44, 47, 49-52, 54 and 56-58 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Pouletty *et al.* (WO 95/10302).

Pouletty *et al.* teach bifunctional reagents or conjugates of an anchor and a physiologically active entity (the first binding entity or target binding member), where the reagent is bound through an anchor to a long lived moiety associated with the blood, either cellular or a mobile blood protein (page 2, lines 8-14; claims 44, 47). The anchor and the target binding moiety can be connected by covalent bond in a single member conjugate (page 13, lines 29-35), and the two can also be covalently linked by an appropriate chain (page 27, lines 12-15; claim 51). Binding of the reagent to the long-lived blood protein may be specific or covalent (page 11, lines 29-35; clam 52, 54), and the functional groups on the protein are amino, carboxyl, and thiol groups which can be used as the target for reactive functionality of the reagent to form amide, ester and disulfide, and a number of bifunctional compounds for linking to entities are provided (page 17, line 32-page 19, line 1; Examples; claims 49-50 and 56-58). The first binding entity may be a ligand for a naturally occurring receptor, a substrate for an enzyme (page 20, lines 14-17). Thus, the reference makes obvious if not anticipated to the claimed method for

identifying a drug containing an anchoring moiety, which binds a target site of a biological molecule.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

19. Claims 59-62 are rejected under 35 U.S.C. 102(e) as being anticipated by Fesik *et al.* (U. S. Patent 5,989,827, filed October 1996).

Fesik *et al.* teach a method for identifying compounds as new drug leads, which bind to a given target biomolecule (e.g., protein). The method comprises identifying a first ligand to the target molecule using two-dimensional $^{15}N/^{1}H$ NMR correlation spectroscopy; identifying a second ligand to the target molecule using two-dimensional $^{15}N/^{1}H$ NMR correlation spectroscopy; forming a ternary complex by binding the first and second ligands to the target molecule; determining the spatial orientation of the first and the second ligands on the target molecule; and linking the first and second ligands to form a drug using an appropriate linking

group to maintain the spatial orientation (column 2, lines 33-62; Examples 1-5; claim 59). The first and second ligands can be selected from a collection of compounds on the basis of size and molecular diversity (column 8, lines 25-36; clims 60 and 61).

Conclusion

20. No claims are allowed.

Art of Record

It appears that there is no prior art related to the method of identifying a drug (A-L-D) of a local anesthetic such as benzocaine derivative containing a methanethiosulfonyl group as an anchoring group, which covalently binds to the sodium channel.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

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April 16, 2002